



Application Note AN-U-076

USP 総則 <591>1)に準拠した酸化亜鉛の分析

USP monograph modernization utilizing ion chromatography as a valid analysis method

Zinc is an essential trace element which is used in different pharmaceuticals and supplements [1]. In the form of zinc oxide, zinc is an integral part of skin care creams, pastes, and supplements [2,3]. In order to meet the stringent quality standards for pharmaceutical products, manufacturers and laboratories must employ validated methods as from the United States Pharmacopeia and National Formulary (USP-NF). In the course of their modernization activities, USP-NF also updated the zinc monograph and replaced the existing identification procedure

with titration by ion chromatographic analyses. Ion chromatography (IC) qualified as a methodical approach for the zinc assay in General Chapter <591>, Zinc Determination [4]. The analysis involves separation of zinc using, e.g., L91 column material (Metrosep A Supp 10) followed by post-column reaction using 4-(2-pyridylazo)resorcinol (PAR) and subsequent detection at 530 nm. IC was validated according to USP procedures as a highly specific and accurate method to ensure product safety and quality.

SAMPLE AND SAMPLE PREPARATION

All analyses are performed with a solution of ultrapure zinc oxide. No additional sample

preparation is required unless stated in the individual USP monographs.

EXPERIMENTAL

A sample stock solution is prepared by hydrolyzing 0.1868 g of ultrapure zinc oxide powder in 10 mL of 6 mol/L hydrochloric acid. This solution is made up to 100 mL in a volumetric flask with ultrapure water. The zinc concentration of this sample stock solution corresponds to 1500 µg/mL. To prepare the final sample solution, the sample stock solution is diluted 1:100 with 0.2% (w/v) HCl to obtain a final concentration of 15 µg/mL zinc. The working standard solution is prepared from a certified 1000 µg/mL zinc standard.

Samples and standard solutions were injected directly into the IC (Figure 1) using an 889 IC Sample Center – cool. Zinc is separated from all other cations using L91 column material (Metrosep A Supp 10 - 250/4.0 and Metrosep A Supp 10 Guard/4.0) applying the MetPac™ PDCA (pyridine-2,6-dicarboxylic acid) eluent (concentrate dilution 1:5) followed by post-column reaction (PCR) with MetPac™ PAR and subsequent detection at a wavelength of 530 nm.



Figure 1. Instrumental setup including a 930 Compact IC Flex with a 947 Professional UV/VIS Detector Vario, a 800 Dosino for PCR delivery and mixing, and an 889 IC Sample Center – cool. Cooling can prolong sample stability.

The calibration was performed using a single 15 µg/mL zinc standard injected six times. The

sample was analyzed in duplicate.

Table 1. Requirements for IC method as per USP General Chapter <591>.

Column with L91 packing	Metrosep A Supp 10 - 250/4.0
Eluent	MetPac™ PDCA concentrate (dilution 1:5)
Flow rate	1.2 mL/min
Temperature	30 ° C
Injection volume	10 µL
PCR reagent	PAR (0.12 g MetPac™ PAR reagent in 1000 mL MetPac™ PAR diluent)
PCR flow rate	0.6 mL/min
Detection	Vis: 530 nm after PCR

RESULTS

The IC assay for zinc content was validated according to USP General Chapter <591>, Zinc Determination [4]. Ultrapure zinc oxide was analyzed for its zinc content. The accuracy of the zinc determination was calculated as 99% (Figure 2).

All acceptance criteria were fulfilled, e.g., asymmetry (tailing factor) for the zinc peak was <2, or the relative standard deviation of the standard solutions was <0.73% (n = 6, USP requirement no more than (NMT) 0.73) (Table 2).

Table 2. Required acceptance criteria according to General Chapter <591>.

Parameter	Actual	USP requirement	Status
% RSD	0.582	NMT 0.73	Pass
Tailing factor	1.465	NMT 2.0	Pass
Result standard	98.9%	+/- 2%*	Pass
Results sample	99.2%	+/- 2%*	Pass



Figure 2. Chromatogram of zinc in a zinc oxide sample containing 14.865 $\mu\text{g/mL}$ Zn (99.1% recovery of the nominal concentration).

CONCLUSION

Ion chromatography qualifies for the determination of zinc as per USP General Chapter <591>. Using the column material L91, zinc can be reliably determined in pharmaceuticals and other samples using IC with post-column reaction and UV detection.

The high degree of automation possibilities for

IC systems from Metrohm (e.g., autosampler, Metrohm intelligent Partial Loop injection Technique, Inline Dilution, etc.) and the traceability of all steps during analysis make it a user-friendly, efficient, and valuable analytical technique for pharmaceutical quality control processes.

REFERENCES

1. Royal Society of Chemistry. *Zinc*. The Royal Society of Chemistry's interactive periodic table. <https://www.rsc.org/periodic-table/element/30/zinc>.
2. Juch, R. D.; Rufli, T.; Surber, C. Pastes: What Do They Contain? How Do They Work? *Dermatology* **1994**, 189 (4), 373–377. <https://doi.org/10.1159/000246882>.
3. Maier, T.; Korting, H. C. Sunscreens - Which and What For? *Skin Pharmacol Physiol* **2005**, 18 (6), 253–262. <https://doi.org/10.1159/000087606>.
4. U. S. Pharmacopeia/National Formulary. <591> Zinc Determination. In *General Chapter*, USP/NF, Rockville, MD, USA. https://doi.usp.org/USPNF/USPNF_M9935_0_05_01.html.

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CONFIGURATION



930 Compact IC Flex Oven/ChS/PP/Deg

930 コンパクト IC Flex Oven/ChS/PP/Deg はカラムオープン、ケミカルサプレッション、サプレッサー再生のためのペリスタリックポンプ、内蔵式脱気装置を備えたインテリジェントコンパクトIC装置です。この装置は任意の分離メソッドおよび検出メソッドによって使用することができます。

典型的な使用領域:

- ケミカルサプレッションと電気伝導度検出器による陰イオンの測定
- イオン排除クロマトグラフィーおよび逆のサプレッションを用いた有機酸



889 IC Sample Center – cool

889 IC サンプルセンタ – cool は、使用できるサンプルがごく少量である場合の適切なオートメーションのソリューションです。889 IC サンプルセンタに対して本製品は更に冷却機能を有しているので、生化学的に重要な、または熱化学的に不安定なサンプルに最適なサンプルチェンジャーです。



947 Professional UV/VIS Detector Vario SW

インテリジェントな単一波長検出器 947 Professional UV/VIS Detector Vario SW は、紫外線や可視光線範囲でアクティブな物質を安全かつ確実に検出することができます。波長を一つ選択することができます。



Metrosep A Supp 10 - 250/4.0

分離カラムMetrosep A Supp 10 - 250/4.0は粒子径たった4.6 μm の大容量ポリスチレン・ジビニルベンゼン共重合体をベースとしています。A-Supp-10シリーズで最長のこのカラムは、最高の選択性と柔軟性を提供します。クロマトグラムの時間が長い場合は特に、MSM-HCの使用が推奨されます。この分離カラムにおいても、温度、流量、溶離液の構成成分の変化による陰イオンの様々な分離が可能です。

Metrosep A Supp 10 - 250/4.0は非常に大きな容量を備えています。これは、イオン強度の高いサンプル、複雑な分離課題、個々の成分濃度に大きな差異のあるサンプルの分析に適しています。



Metrosep A Supp 10 Guard/4.0

Metrosep A Supp 10 Guard/4.0は分析用分離カラムMetrosep A Supp 10を効果的に汚れから守ります。この保護カラムは「On Column Guard System」によってとりわけ取り扱いが大変容易な点において優れています。保護カラムは、直接簡単に分析用カラムに回して取り付けられます。工具は必要ありません。